



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

70

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,461	12/11/2003	Michael P. Czech	UMY-055	3119
959 7590 10/03/2007 LAHIVE & COCKFIELD, LLP ONE POST OFFICE SQUARE BOSTON, MA 02109-2127			EXAMINER SCHNIZER, RICHARD A	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 10/03/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/735,461	Applicant(s) CZECH ET AL.	
	Examiner Richard Schnizer, Ph. D.	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27 and 38-86 is/are pending in the application.
- 4a) Of the above claim(s) 60-78 and 80 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27,38-59,79 and 81-86 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>7/9/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/22/07 has been entered.

Claim 86 was added as requested.

Claims 60-78 and 80 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/22/06.

Claims 27, 38-59, 79, and 81-86 are under consideration in this Action. Claim 81 is considered only to the extent that it depends from claim 79.

Rejections Withdrawn

Applicants amendments overcame the rejection of claims 27, 38-59, 79, and 81-85 under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 27, 38-48, 50, 51, 56-59, 79, and 81-86 are rejected under 35 U.S.C.

103(a) as being unpatentable over Al-Hasani et al (J. Biol. Chem. 273(28): 17504-17510, 1998) in view of Clancy et al (US 20030087259) and Paquereau et al (Anal. Biochem. 204(1): 147-151, 1992).

Al Hasani taught methods of studying genes related to glucose transport. Specifically, Al-Hasani investigated the relationship between the GTPase dynamin and endocytosis of the GLUT4 glucose transporter in cultured rat adipocytes. Adipocytes were transfected by electroporation with a construct for expressing an easily detectable (HA)-tagged GLUT4, and then with either constructs for over-expression of either wild type dynamin or a GTPase-negative mutant of dynamin. Voltage was 0.2 kV. The effects of these dynamins on (HA)-tagged GLUT4 endocytosis after insulin treatment was measured. See abstract, paragraph bridging pages 17505 and 17506, Fig. 2 on page 17506, and Fig. 3 on page 17507.

Al Hasani did not teach the use of siRNA and was silent as to the capacitance setting for use in electroporation

Clancy taught that the activity of a polypeptide in a cell can be controlled by several alternative means including the use of negative mutants of the protein and the use of antisense or siRNA directed at the mRNA encoding the protein. See summary of invention paragraph 9, detailed description paragraph 234, and claim 21.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use siRNA directed against dynamin to assess its role in the endocytosis of GLUT4. For example, one could have used anti-dynamin siRNA to down-regulate wild type dynamin activity instead using the negative dynamin mutant. This experiment would result in down regulation of the endogenous dynamin (as required by instant claim 59) and the exogenous dynamin expressed from the expression construct (as required by instant claim 58). Further, one of ordinary skill in the art appreciates that the effects of the negative dynamin mutant could be confirmed by reversing them through the use of siRNA directed against the mutant. It would have been obvious to deliver the siRNA by electroporation because Al-Hasani demonstrated that this method was suitable for delivering nucleic acids to adipocytes. However, these references were silent as to the capacitance used for electroporation.

Paquereau taught a method of delivering nucleic acids to mammalian cells by electroporation using a potential of 0.15-0.2 kV and a capacitance of 960 micro F. These conditions minimized cell damage and increased cell survival. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to optimize the electrical potential and capacitance used in the electroporation of the cells of Al-Hasani because it was recognized in the art that these variables could affect the amount of cell damage caused by electroporation, as well as cellular survival after electroporation. In so doing, one of ordinary skill would have noted that Al-Hasani used a voltage in the range used by Paquereau, and so would have been motivated to use a capacitance in the range used by Paquereau with the reasonable expectation of

obtaining minimal cellular damage and improved cellular survival. Note that Paquereau used the exact capacitance required by instant claim 43.

Regarding claims 44-46, the temperature of electroporation, and the time between electroporation and assay, are considered to be variables that are routinely optimized by those of ordinary skill in the art, and so are considered to be obvious.

Claims 53-55 are included in the rejection because these claims, which require increased siRNA stability, or increased or decreased siRNA activity, recite no standard against which to compare stability or activity. One of ordinary skill in the art possesses the ability to modify a given siRNA to have greater or lesser activity and stability by incorporation of a greater or lesser number of modified bases. So, any given siRNA has greater or lesser activity than a differently modified one. In the absence of any standard of comparison these limitations carry no weight.

Claim 56 is included in the rejection because those of ordinary skill in the art appreciate that glucose metabolism is important in a variety of human diseases including diabetes. As a result it would be obvious to perform similar experiments in human cells.

Regarding claims 82 and 83, the concentrations of cells and siRNAs in the electroporation mixture are considered to be result-effective variables that are routinely optimized by those of ordinary skill in the art. Note that Al Hasani electroporated 200 microliters of cells at a concentration of $5-6 \times 10^6$ cells per ml, i.e. about 1 million cells.

Claim 49 is are rejected under 35 U.S.C. 103(a) as being unpatentable Al-Hasani et al (J. Biol. Chem. 273(28): 17504-17510, 1998) in view of Clancy et al (US 20030087259) and Paquereau et al (Anal. Biochem. 204(1): 147-151, 1992), as applied to claims 27, 38-48, 50, 51, 56-59, 79, and 81-86 above, and further in view of Standaert et al (J. Biol. Chem. 272(48): 30075-30082, 1997).

The teachings of Al-Hasani, Clancy, and Paquereau are summarized above and can be combined to render obvious methods of identifying a gene that affects glucose transport by assaying insulin-mediated GLUT4 translocation in the presence or absence of dynamin, wherein dynamin concentration is modulated through siRNA delivered by electroporation at 0.15-0.2 kV and 960 microFarads.

The references do not teach an assay of glucose uptake.

Standaert taught method of studying the effect of a gene expression of protein kinase C zeta (PKC-zeta) on glucose transport. Assays included measurement of GLUT4 translocation as well as glucose uptake. See abstract, paragraphs bridging pages 30078 to 30080, and Figs 7 and 8 on page 30079.

It would have been obvious to one of ordinary skill in the art at the time of the invention to extend the studies of Al-Hasani to studies of glucose uptake. One of ordinary skill in the art, interested in the effects of genes on glucose transport, would have realized that GLUT4 translocation and GLUT4 transport activity can both be used as measures of the effect of a gene product on glucose transport, and would have been motivated to use either one. However, one would have been particularly motivated to assay glucose uptake directly given that is the actual function of GLUT4, and so would

provide a more accurate representation of the effects of the gene product on glucose transport.

Claims 52-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Al-Hasani et al (J. Biol. Chem. 273(28): 17504-17510, 1998) in view of Clancy et al (US 20030087259) and Paquereau et al (Anal. Biochem. 204(1): 147-151, 1992), as applied to claims 27, 38-48, 50, 51, 56-59, 79, and 81-86 above, and further in view of McSwiggen et al (US Patent 7,022,828).

The teachings of Al-Hasani, Clancy, and Paquereau are summarized above and can be combined to render obvious methods of identifying a gene that affects glucose transport by assaying insulin-mediated GLUT4 translocation in the presence or absence of dynamin, wherein dynamin concentration is modulated through siRNA delivered by electroporation at 0.15-0.2 kV and 960 microFarads.

The references do not teach siRNA derivatives.

McSwiggen taught methods of inhibiting gene expression using siRNA, and taught that the stability of siRNA molecules could be enhanced through the use of modified bases. See and column 25, lines 58-67 claim 1.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use modified siRNA oligonucleotides in the invention of Al-Hasani as modified by Clancy and Paquereau. One would have been motivated to do so in order to enhance the function of the oligonucleotides, as taught by McSwiggen.

Response to Arguments

Applicant's arguments, and the Declaration of inventors Czech, Zhou, and Jiang under 37 CFR 1.132, filed 8/22/07 have been fully considered but they are not persuasive.

Applicant addresses the obviousness rejections at pages 13-23 of the response. Applicant argues and declares that one of skill would have found neither a reasonable expectation of success, nor the motivation to arrive at the claimed invention. This is unpersuasive because it was clear to those of ordinary skill in the art at the time of the invention that adipocytes could be transfected by electroporation, it was routine in the art at that time to optimize electroporation conditions, and the conditions used by Applicant to obtain siRNA delivery were conditions that were routinely used in the prior art for the delivery of nucleic acids to mammalian cells (see Al-Hasani and Paquereau above).

Applicant argues and declares that the claims are non-obvious because they now require expression of the target gene to be reduced by at least 70% in the culture of adipocytes. This is unpersuasive. It is well accepted in the art, and apparent from the teachings of Weil and Walters (cited previously by Applicant) that the conditions of electroporation of mammalian cells were result effective variables that were obvious to optimize. Note that, while silent as to capacitance, Al-Hasani taught a voltage (0.2 kV) for electroporating adipose cells that is squarely in the center of the range claimed by Applicant. Further, Paquereau combined a voltage in the range of 0.15 to 0.2 kV and a capacitance of 960 microFarads for electroporating mammalian cells, the exact

conditions used by Applicant to achieve 70% reduction in expression. So, it is clear that the values of voltage and capacitance used by Applicant to achieve electroporation were routinely used by those of ordinary skill prior to the invention for the purpose of electroporating nucleic acids into mammalian cells. One of ordinary skill seeking to electroporate siRNA into adipocytes would reasonably have started with the voltage that Al-Hasani used for adipocytes, and then optimized the capacitance. In view of the teachings of Paquereau, 960 microFarads was routinely used in the transfection of mammalian cells. So one of ordinary skill would have arrived at the instantly claimed electroporation conditions through routine optimization.

Applicant argues that it is essential to the invention that the adipocyte population exhibit sufficient reduction in expression of the targeted gene to be able to reliably assay that gene's effect on glucose transport. Applicant further declares that "it was well known in the art at the time of filing that electroporation of DNA into adipocytes only leads to the successful expression of DNA in only a small minority of the adipocytes" (approximately 1-10%, relying on page 40 of the instant specification for support). "In contrast, in order for siRNA to successfully silence the gene of interest, *i.e.*, mediate RNA interference, as currently claimed, it is required that virtually all of the adipocytes (***approximately 100%***) take up functional siRNA." Applicant concludes that since the successful electroporation of DNA into adipocytes was typically less than 10% efficient, it would not have been obvious to one of ordinary skill in the art at the time of filing of the instant invention that electroporation of siRNA into adipocytes could be nearly 100% efficient.

To the extent that this is an argument of unexpected results, it is unpersuasive because the claims are not commensurate in scope with the results obtained. The results were obtained using specific electroporation conditions that are recited only in claim 43, and so could be persuasive only with regard to claim 43 and not for the other, broader claims. Applicant's argument is not persuasive regarding claim 43 for the following reasons. First, it is based in part on the assertion that, "in order for siRNA to successfully silence the gene of interest, *i.e.*, mediate RNA interference, as currently claimed, it is required that virtually all of the adipocytes... take up functional siRNA." This assertion does not appear to be true. Al Hasani was capable of studying the effect on GLUT4 intracellular recycling by recombinant expression of GLUT4 and either GTPase dynamin or a GTPase-negative dynamin. Rat adipocytes were transfected with expression vectors encoding GLUT4 and either of the dynamins, and the effects on GLUT4 translocation in the presence of insulin were observed. See abstract. Note that instant claim 50 explicitly identifies measuring insulin-mediated GLUT-4 translocation as a means of assaying glucose transport. Applicant has not explained why 100% transfection efficiency would be required when studying glucose transport using siRNA to downregulate a cellular process, when 10% efficiency (or far less) was sufficient for studying the same process by transfection of separate expression vectors encoding GLUT4 and dynamin.

Applicant asserts and declares that a skilled artisan would not have reasonably expected that mere substitution of siRNA for plasmid DNA would lead to success in an

electroporation method. For support Applicant relies on Walters (2002) and Weil (2002).

Walters taught that the effectiveness of siRNA may depend on transfection technique. Specifically, the results of Walters indicated that siRNAs delivered using cationic lipid transfection techniques were sequestered in the endosome/lysosome pathway in a nonadherent cell line, KAS-6/1 human myeloma cells. See page 417, column 1, first full paragraph. In order to circumvent this problem, Walters used electroporation to deliver the siRNAs because it was known in the prior art that electroporation allowed direct delivery to the cytosol and did not depend on the endosome/lysosome (endocytic) pathway. This provides evidence that it was routine in the art at the time of the invention to optimize transfection protocols to determine which protocol worked best for a given cell line. It does not provide any evidence that one of ordinary skill in the art would not have had a reasonable expectation of success in obtaining RNAi in adipocytes by electroporating siRNAs. Accordingly, Applicant's reliance on Walters is misplaced.

The Weil reference is relied upon to teach that "the first difficulty in implementing RNA interference with a new cell type is optimizing the transfection process." However, this is essentially an admission that it is simply a matter of optimization, particularly in view of the fact that it was well known in the art that molecules could be electroporated into adipocytes (Al-Hasani, of record, and Zhang, above). Weil also suggested that electroporation of siRNAs can be efficient for nonadherent cells, and stated that the optimal parameters for the electroporation of siRNA differ from those of plasmids,

Art Unit: 1635

allowing the use of milder conditions that induce less cell toxicity. See abstract. Weil does not provide any evidence that one of ordinary skill in the art would not have had a reasonable expectation of success in obtaining delivering siRNA to adipocytes by electroporation. Instead, Weil provides some motivation for selecting electroporation as a delivery technique for nonadherent cells, stating at page 1247, column 3, that for cells growing in suspension, calcium phosphate precipitation is inappropriate, and liposomes and cationic lipids are unpredictable on new cell lines, whereas electroporation "can, a priori, be adapted to all cell types".

Note also that in optimizing the electroporation parameters, Weil used the combinations of 0.3 kV/ 125 microFarads; 0.28 kV /250 microFarads; and 0.26 kV/960 microFarad (see page 1245, column 1, last paragraph). Only claims 41-43 recite a parameter not anticipated by Weil. These claims recite capacitance in the range examined by Weil, but have voltages slightly outside the range of Weil. However, in view of the range of voltages embraced by the claims, one of ordinary skill would be led to believe that the voltage parameter is not critical outside a range of 0.01 kV to 2.0 kV when using capacitance of 960 microFarads. Accordingly, Weil only provides further evidence of the obviousness of each of the instant claims.

Applicant argues and declares that the art is replete with teachings indicating that adipocytes are recognized as difficult to transfect. This is true, however it does not change the fact that it was known that adipocytes could be electroporated, the fact that electroporation conditions were routinely optimized, or the fact that the precise conditions used by Applicant were applied to other mammalian cells in the prior art.

Art Unit: 1635

Accordingly it would have been obvious to one of ordinary skill in the art to arrive at the claimed electroporation conditions in the course of routine optimization.

Applicant's arguments regarding motivation, set forth at pages 18 and 19, are reiterated from previous responses received 12/12/06 and 7/25/07 and are unpersuasive for the reasons of record in the Final Rejection of 2/22/07. Specifically, MPEP 2144.06 indicates that when it is recognized in the art that elements of an invention can be substituted, one for the other, while retaining essential function, such elements are art-recognized equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In this case, Clancy taught that the activity of a polypeptide in a cell can be controlled by several alternative means including the use of negative mutants of the protein and the use of antisense or siRNA directed at the mRNA encoding the protein. See summary of invention paragraph 9, detailed description paragraph 234, and claim 21. Substituting one of these means for another is obvious, and requires no express suggestion in light of MPEP 2144.06. Accordingly, Applicant's argument that there is no motivation to select a specific member of the antagonists recited by Clancy is unpersuasive. Applicant also argues that one of ordinary skill would not have relied upon Clancy for any teaching because Clancy relates to diagnostic and therapeutic methods related to bone and cartilage formation, not glucose transport. This is unpersuasive because Clancy's general teaching that there exists a variety of alternative means to negatively control a polypeptide in a cell is not limited to

the context of bone and cartilage formation and one of ordinary skill in the art would clearly understand that it is applicable to polypeptides in general.

At pages 20 and 21, Applicant addresses the rejection over the Paquereau reference. Applicant argues that siRNAs are different entities from the plasmids of Paquereau, as are adipocytes and hepatocytes, such that one of skill in the art would not have had a reasonable expectation of success in utilizing the parameters of Paquereau for delivery of siRNAs. This is unpersuasive because, as discussed above, transfection conditions are routinely optimized by those of skill in the art. Applicant has presented no evidence that electroporation conditions used for plasmids would not function for siRNAs. In fact, Weil suggested only that substitution of siRNA for plasmids simply allows one to use milder conditions that induce less cell toxicity. See abstract. Weil also taught that electroporation can be adapted to all cell types. Because it is routine in the art to optimize transfection parameters, and the prior art taught that electroporation could be adapted to all cell types, there is no reason for one of ordinary skill to lack a reasonable expectation of success. Similarly, since Paquereau exemplified 960 microFarads capacitance for mammalian cells, one of ordinary skill would be motivated to use that capacitance as a starting point in the process of optimization.

Applicant addresses the Standaert reference at page 22, arguing essentially that it fails to rectify the deficiencies of the Al Hasani and Clancy references. This is unpersuasive for the reasons set forth above regarding these references.

Art Unit: 1635

Applicant addresses the McSwiggen reference at page 23. Applicant argues that it fails to rectify the deficiencies of the Al Hasani and Clancy references. This is unpersuasive for the reasons set forth above regarding these references. Applicant also asserts that there is no motivation to combine this reference with Al Hasani and Clancy because McSwiggen is directed to siRNA derivative chemistry and not to the art of glucose transport. This is unpersuasive because McSwiggen was not relied upon to teach glucose transport. Al Hasani taught study of glucose transport by inhibiting the activity of a dynamin gene product through the use of a dominant negative mutant. In view of the teachings of Clancy, one of ordinary skill appreciates that there are several alternative, exchangeable ways to inhibit the activity of a gene product, including inhibiting transcription of the gene, e.g. by siRNA. McSwiggen taught methods of inhibiting gene expression using siRNA, and taught that the stability of siRNA molecules could be enhanced through the use of modified bases. Thus there is clear motivation to modify siRNAs to make them more stable, and it would have been obvious to do so in the method of Al Hasani as modified by Clancy and Paquereau.

For these reasons the rejections are considered proper.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the

Art Unit: 1635

hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

A handwritten signature in black ink, appearing to read 'Richard Schnizer', with a stylized flourish at the end.

Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635